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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1.53(b))

Attorney Docket No.	22920.0003
First Inventor	John A. GIORDANO et al.
Title	METHOD AND COMPOSITION FOR SUPPLEMENTATION OF NUTRITIONAL DEFICIENCIES IN RENAL PATIENTS
Express Mail Label No.	N/A

APPLICATION ELEMENTS

See MPEP Chapter 600 concerning utility patent application contents.

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Washington, DC 20231

1. [X] Fee Transmittal Form
   (Submit an original and a duplicate for fee processing)
2. [X] Applicant claims small entity status.
   See 37 CFR 1.27.
3. [X] Specification [*Total Pages* 28]
   (preferred arrangement set forth below)
   - Descriptive title of the invention
   - Cross Reference to Related Applications
   - Statement Regarding Fed sponsored R&D
   - Reference to sequence listing, a table, or a computer program listing appendix
   - Background of the Invention
   - Brief Description of the Drawings (if filed)
   - Detailed Description
   - Claim(s)
   - Abstract of the Disclosure
4. [ ] Drawing(s) *(35 USC 113)* [*Total Sheets* 0]
5. Oath or Declaration [*Total Pages* 2]
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   b. [ ] Copy from a prior application (37 CFR 1.63(d))
      (for continuation/divisional with Box 17 completed)
      i. [ ] DELETION OF INVENTOR(S)
      Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b).
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ACCOMPANYING APPLICATION PARTS

9. [X] Assignment Papers (cover sheet & documents(s))
10. [ ] 37 CFR 3.73(b) Statement [ ] Power of Attorney
    (when there is an assignee)
11. [ ] English Translation Document *(if applicable)*
12. [ ] Information Disclosure Statement (IDS)/PTO-1449 [ ] Copies of IDS Citations
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of:

John A. GIORDANO et al.

Application No.: Unassigned

ATTN: BOX PATENT APPLICATION

Filed: 27 September, 2000

For: METHOD AND COMPOSITION FOR SUPPLEMENTATION OF NUTRITIONAL DEFICIENCIES IN RENAL PATIENTS

PATENT OFFICE FEE TRANSMITTAL LETTER

Commissioner for Patents
Washington, D.C. 20231

Sir:

The following fees are enclosed in connection with the filing of the attached papers:

Utility Application Filing Fee	**$1,365.00**
Assignment Recordal Fee	**$ 40.00**

It is not believed that any further fees are due in connection with the filing of the attached papers. However, the Commissioner is authorized to charge any underpayment or credit any overpayment of fees to the deposit account of undersigned, no. 50-1067.

Respectfully submitted,

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Applicant or Patentee: John A. GIORDANO et al. Atty. Docket. No. 22920.0003

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) AND 1.27 (c)) - SMALL BUSINESS CONCERN

I hereby declare that I am

( ) the owner of the small business concern identified below:

(X) an official of the small business concern empowered to act on behalf of the concern identified below:

NAME OF CONCERN Everett Laboratories, Inc.
ADDRESS OF CONCERN 29 Spring Street, West Orange, New Jersey 07052

I hereby declare that the above-identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18 and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled METHOD AND COMPOSITION FOR SUPPLEMENTATION OF NUTRITIONAL DEFICIENCIES IN PATIENTS by inventor(s) John A. GIORDANO and Charles BALZER described in

(X) the specification filed herewith
( ) application serial no. , filed
( ) patent no. , issued

If the rights held by the above-identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e).

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I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate: (37 CFR 1.28(b)).

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING: EVERETT FELPER
TITLE OF PERSON OTHER THAN OWNER: PRESIDENT
ADDRESS OF PERSON SIGNING: 29 SPRING STREET, WEST ORANGE, NJ
SIGNATURE: Everett Felper DATE: 9/25/00

METHOD AND COMPOSITION FOR SUPPLEMENTATION OF NUTRITIONAL DEFICIENCIES IN RENAL PATIENTS

FIELD OF THE INVENTION

The present invention relates to compositions comprising various vitamins and minerals, and methods for using these compositions for the treatment of renal disease and associated disorders.

BACKGROUND OF THE INVENTION

The kidney has three major physiological functions: excretory, endocrine, and metabolic. However, regulation and excretion of water, minerals, and other nutrients is the most important function of the kidneys. Metabolic waste products eliminated by the kidneys include urea, creatinine, uric acid, hemoglobin degradation products, and hormone metabolites. The kidneys also play a role in arterial pressure regulation by secreting vasoactive substances such as renin. In addition, the kidneys secrete erythropoietin, which stimulates red blood cell production, and produce 1,25-dihydroxy vitamin D_3, the active form of vitamin D. Any of these functions may be impaired in renal disease leading to disruptions in the nutritional status of the patient. TEXTBOOK OF MEDICAL PHYSIOLOGY 315 (Guyton & Hall, 9th ed. 1996).

Renal disease is one of the leading causes of morbidity, with millions of individuals affected annually. Generally, renal disease may be classified into two categories: 1) acute renal failure and 2) chronic renal failure. Acute renal failure is characterized by a sudden reduction or cessation of renal function. In contrast, chronic renal failure refers to a progressive loss of renal function, usually a result of an underlying pathological condition. For example, immunological disorders such as lupus erythematosus, metabolic disorders such as diabetes mellitus and hypertension, and infectious diseases such as tuberculosis can lead to chronic renal failure. As renal function continues to deteriorate, patients develop end-stage renal failure (ESRD) that eventually requires dialysis treatment or transplantation. *Id.*, at 413.

Patients with chronic renal failure typically develop generalized edema, acidosis, and uremia, an accumulation of nitrogenous metabolites in the blood. To alleviate these symptoms,

patients are placed on dietary therapy or dialysis. The protein-restricted diet prescribed for renal patients is generally deficient in vitamins such as folate, the B vitamins, and vitamin C. HANDBOOK OF NUTRITION AND THE KIDNEY 42 (Mitch & Klahr, eds., 3rd ed. 1998) (hereinafter "HANDBOOK"). In addition, the dialysis procedure itself may remove vitamins and nutrient compounds. Gastrointestinal absorption of vitamins may be also altered in patients suffering from chronic renal failure. Makoff, 25 MINER. ELECTROLYTE METABOL. 349-351 (1999).

Compliance with the restrictive renal diet may also result in deficiencies in trace minerals such as zinc and selenium. Highly protein-bound minerals may be lost in excessive amounts in patients with proteinuria. Zima et al., 17 BLOOD PURIF. 182-186 (1999). Furthermore, it has been shown that plasma levels of selenium are decreased in dialysis patients. HANDBOOK, at 43. Poor nutritional status and insufficient levels of vitamins and minerals may place renal patients at higher risk for diseases such as anemia, infections, and cardiovascular disease, or aggravate pre-existing conditions such as hyperlipidemia, osteoporosis, and viral hepatitis. MODERN NUTRITION IN HEALTH AND DISEASE 1447 (Shils et al., eds., 9th ed. 1999).

Nutritional intervention is critical to the management of chronic renal disease and end-stage renal disease. Dietary therapy should maintain or improve the nutritional status of the renal patient and minimize or prevent uremic and metabolic toxicities associated with renal failure. The challenge is to simplify a complex dietary regimen while providing an effective nutritional treatment. The nutritional compositions and related methods described herein includes the numerous vitamins and minerals deficient in the restricted diet of the renal patient. Thus, the composition and method of the present invention offers a means to meet the nutritional needs of the renal patient in an uncomplicated approach.

SUMMARY OF THE INVENTION

The present invention provides nutritional compositions and methods of using said compositions for treating patients with renal disease. Specifically, the present invention discloses novel compositions of vitamins and minerals in an amount that can be used to supplement the nutritional deficiencies observed in patients afflicted with renal disease, renal insufficiency, or end-stage renal disease. The compositions of the present invention can also be used as nutritional supplements for patients undergoing dialysis therapy or for patients on a restricted diet. In addition, the compositions can be used to treat the nutritional deficiencies of

any disease state that results in increased oxidative stress, elevated cholesterol levels, or elevated homocysteine levels.

The compositions of the present invention comprise numerous vitamins and minerals that will improve the nutritional state of a patient. The vitamins of the present invention preferably comprise vitamin C, vitamin E, vitamin B_1, vitamin B_2, vitamin B_3, vitamin B_5, vitamin B_6, vitamin B_{12}, biotin, and folic acid. The minerals of the present invention preferably comprise chromium, selenium, and zinc.

In a preferred embodiment, the composition comprises about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.7 mg to 3.3 mg thiamine (vitamin B_1), 1.8 mg to 2.25 mg riboflavin (vitamin B_2), 18 mg to 22 mg niacin (vitamin B_3), 9 mg to 11 mg pantothenic acid (vitamin B_5), 13.5 mg to 16.5 mg pyridoxine (vitamin B_6), 10.8 μg to 13.2 μg cyanocobalamin (vitamin B_{12}), 270 μg to 330 μg biotin, 2.25 mg to 2.75 mg folic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, and 18 mg to 22 mg zinc.

In a further preferred embodiment of the present invention, the composition comprises 50 mg of vitamin C, 35 IU vitamin E, 3 mg of thiamine, 2 mg of riboflavin, 20 mg of niacin, 10 mg of pantothenic acid, 15 mg of pyridoxine, 12 μg cyanocobalamin, 300 μg of biotin, 2.5 mg of folic acid, 200 μg of chromium, 70 μg of selenium, and 20 mg of zinc.

The present invention also relates to methods for supplementing the nutritional deficiencies in a patient comprising the step of administering to said patient a composition comprising vitamin C, vitamin E, B-complex vitamins, chromium, selenium, and zinc. The compositions used in the methods of the present invention may further comprise a pharmaceutically acceptable carrier. In a preferred embodiment, the compositions of the present invention are administered to said patient orally and preferably on a daily basis.

In another embodiment of the compositions of the present invention, vitamin C comprises ascorbic acid, vitamin E comprises d-alpha tocopheryl succinate, pantothenic acid comprises d-calcium pantothenate, niacin comprises niacinamide, selenium comprises L-selenomethionine, zinc comprises L-Optizine ZML-200 InterHealth™, chromium consists of chromium chloride, chromium picolinate, and chromium tripicolinate, and B-complex is one or more vitamins selected from the group consisting of pantothenic acid, cyanocobalamin, niacin, pyridoxine, riboflavin, thiamine, folic acid, and biotin.

DETAILED DESCRIPTION

The nutritional therapy of individuals with renal disease requires a unique formulation due to the multiple metabolic and biochemical changes, as well as dietary restrictions. The prescribed diet restrictions usually result in decreased consumption of vital nutrients such as vitamin C, vitamin E, the B-complex vitamins, and zinc. Rocco et al., 7 J. RENAL NUTR. 17-24 (1997). In addition, patients with end-stage renal disease are often in a uremic state which increases oxidative stress and free radical production, affects the appetite, and alters the body's ability to utilize nutrients. Tetta et al., 17 BLOOD PURIF. 118-126 (1999). The dialysis process may also result in a depletion of essential nutrients. Stein et al., 3 BLOOD PURIF. 52-62 (1985). The novel compositions and related methods of the present invention comprise a unique mixture of vitamins and minerals that are useful as nutritional supplements for treating patients suffering from renal disease.

The term "renal disease" is a generic expression encompassing an array of disorders that afflict the kidneys. The term "renal patient" includes patients suffering from renal disease. In general, renal diseases are categorized according to the affected morphologic component: glomerulus, tubules, and blood vessels. The glomerulus is a network of branching and anastomosing capillaries that filters proteins, toxins, and other substances from the blood. A number of factors may lead to injury to glomeruli including secondary affects from immunologic, vascular, and metabolic diseases. Diseases of the glomerulus include, but are not limited to, glomerulonephritis, nephrotic syndrome, lipoid nephrosis, glomerulosclerosis, Berger disease, and hereditary nephritis. ROBBINS PATHOLOGIC BASIS OF DISEASE 942 (Cotran et al., 6th ed. 1999).

The tubules of the kidney reabsorb components from the glomerulus filtrate into the blood. The epithelial cells of the tubules are particularly sensitive to ischemia and toxins and thus, predispose the tubules to injury. Disease conditions of the tubules include, but are not limited to, acute tubular necrosis, tubulointerstitial nephritis, pyelonephritis, urate nephropathy, and nephrocalcinosis. *Id.*, at 968-980.

The richly vascularized kidney receives approximately 25% of the cardiac output and systemic vascular diseases such as vasculitis and hypertension may have secondary effects on renal blood vessels. Other diseases of the renal blood vessels include, but are not limited to, benign nephrosclerosis, renal artery stenosis, thrombotic microangiopathies, hemolytic-uremic

syndrome, and sickle cell disease nephropathy. *Id.*, at 981-987. In addition, tumors such as oncocytoma and renal cell carcinoma may also impair renal function. *Id.*, at 991-994. Regardless of the origin, the numerous diseases described above eventually culminate in chronic renal disease and ultimately end-stage renal disease.

Reduced levels of serum vitamin C have been observed in chronic renal failure patients. These reduced levels were most likely due to a low-potassium diet and decreased food intake. Marumo et al., 9 INT. J. ARTIF. ORGANS 17-24 (1986). The low-potassium renal diet generally restricts fruit and vegetables which are abundant in potassium and vitamin C. The major biochemical role of vitamin C is as a cosubstrate in metal catalyzed hydroxylations and it has antioxidant properties interacting directly with superoxide hydroxyl radicals and singlet oxygen. In addition, vitamin C provides antioxidant protection for folate and vitamin E. RECOMMENDED DIETARY ALLOWANCES 115 (National Research Council, 10th ed., 1989) (hereinafter "RDA"). One embodiment of the compositions of the present invention provides a supplemental dose of vitamin C, preferably in the amount of about 45 to about 55 mg.

Vitamin E is an antioxidant found in biological membranes where it protects the phospholipid membrane from oxidative stress. RDA, at 99-101. It is also an antiatherogenic agent and studies have demonstrated a reduced risk of coronary heart disease with increased intake of vitamin E. Stampfer et al., 328 N. ENGL. J. MED. 1444-1449 (1993). Decreased levels of vitamin E have been observed in chronic renal failure patients and in patients undergoing dialysis. Taccone-Gallucci et al., 27 CLIN. NEPHROL. 238-241 (1987); Ito et al., 217 JAMA 699 (1971). In addition, it has been demonstrated that the typical renal diet is deficient in vitamin E. Ono, 40 NEPHRON 440-445 (1985). Furthermore, atherosclerotic cardiovascular disease is a leading cause of death in patients with end-stage renal disease. Maiorca, et al., 43 KIDNEY INT. S4-S10 (1993). Thus, one embodiment of the compositions of the present invention provides a supplemental dose of vitamin E, preferably in the amount of about 31.5 to about 38.5 IU.

Thiamine (vitamin B_1) is a coenzyme for the oxidative decarboxylation of α-ketoacids and for transketolase which is a component of the pentose phosphate pathway. The activity of thiamine is inhibited by folate deficiency and malnutrition. RDA, at 123. Chronic renal failure patients placed on a low protein diet exhibited a thiamine deficiency. Porrini et al., 59 INT. J. VITAM. NUTR. RES. 304-308 (1989). In addition, erythrocyte transketolase activity was impaired in dialysis patients. Descombes et al., 43 KIDNEY INT. 1319-1328 (1993). Hence, to correct for

any potential thiamine deficiency in renal patients, one embodiment of the compositions of the present invention may also comprise thiamine, preferably in the amount ranging from about 2.7 to about 3.3 mg.

Riboflavin (vitamin B_2) is a component of two flavin coenzymes, flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD). These flavoenzymes are involved in a number of oxidation-reduction reactions including the conversion of pyridoxine and niacin. RDA, at 132. Renal patients prescribed a low protein diet demonstrated evidence of riboflavin deficiency. Porrini et al., 59 INT. J. VITAM. NUTR. RES. 304-308 (1989); Stein et al., 3 BLOOD PURIF. 52-62 (1985). Corneal vascularization and dermatitis has been noted in patients exhibiting riboflavin deficiency. HANDBOOK, at 116. Thus, one embodiment of the compositions of the present invention may comprise riboflavin, preferably in the amount ranging from about 1.8 to about 2.2 mg.

Nicotinamide adenine dinucleotide (NAD) and NAD phosphate (NADP) are active coenzymes of niacin (vitamin B_3). These coenzymes are involved in numerous enzymatic reactions such as glycolysis, fatty acid metabolism, and steroid synthesis. Niacin is also required for the synthesis of pyroxidine, riboflavin, and folic acid. RDA, at 137. Administration of niacin may also produce a reduction in total cholesterol, LDL, and VLDL levels and an increase in HDL cholesterol. Henkin et al., 91 AM. J. MED. 239-246 (1991). A niacin deficiency was noted in dialysis patients and reduced amounts of niacin have been demonstrated in a low protein renal diet. DeBari et al., 39 AM. J. CLIN. NUTR. 410-415 (1984); Mackenzie et al., 5 PROC. EUR. DIAL. TRANSPLANT. ASSOC. 172-178 (1968). Thus, to maintain appropriate niacin levels in renal patients, one embodiment of the compositions of the present invention may comprise niacin, preferably in the amount ranging from about 18 to about 22 mg.

Pantothenic acid (vitamin B_5) is a component of the coenzyme A macromolecule which is required for the synthesis of fatty acids, cholesterol, steroid hormones, and neurotransmitters. The coenzyme A complex also has a major role in the acetylation and acylation of numerous proteins. RDA, at 169. Low protein diets as typically prescribed for renal patients provide a minimum amount of pantothenic acid. In addition, a decrease in pantothenic acid plasma levels was observed in dialysis patients. Mackenzie et al. 5 PROC. EUR. DIAL. TRANSPLANT. ASSOC. 172-178 (1968). Therefore, to minimize a deficiency of pantothenic acid in renal patients, one

embodiment of the compositions of the present invention may comprise pantothenic acid, preferably in the amount ranging from about 9 to about 11 mg.

The active forms of pyridoxine (vitamin B_6), pyridoxal-5'-phosphate (PLP) and pyridoxamine-5'-phosphate, are coenzymes for numerous enzymes and as such, are essential for gluconeogenesis, niacin formation, and erythrocyte metabolism. RDA at, 142-143. A high incidence of pyridoxine deficiency has been noted in both adult and pediatric chronic renal failure patients, as well as patients undergoing dialysis. Stein et al., 3 BLOOD PURIF. 52-62 (1985); Stockberger et al., 7 NUTR. RES. 1021-1030 (1987); Descombes et al., 43 KIDNEY INT. 1319-1328 (1993). Low protein diets generally have minimal amounts of pyridoxine. Kopple et al., 19 KIDNEY INT. 694-704 (1981). A deficiency in pyridoxine may be attributed to the suppressed immune function observed in chronic renal patients, as well as the increased plasma and tissue oxalate concentrations in renal failure. Dobblestein et al., 5 KIDNEY INT. 233-239 (1974); Morgan et al., 46 NEPHRON 253-257 (1987).

In addition, it has been suggested that pyridoxine deficiency plays a role in homocysteinemia which has been observed in renal patients. Pyridoxine is a coenzyme for both cystathionine synthase and cystathionase, enzymes that catalyze the formation of cysteine from methionine. Homocysteine is an intermediate in this process and elevated levels of plasma homocysteine are recognized as a risk factor for vascular disease. Robinson et al., 94 CIRCULATION 2743-2748 (1996). However, it has been proposed that administration of pyridoxine may reduce the levels of homocysteine. Bostom et al., 49 KIDNEY INT. 147-152 (1996). Hence, one embodiment of the compositions of the present invention may comprise pyridoxine, preferably in the amount ranging from about 13.5 to about 16.5 mg.

Cyanocobalamin (vitamin B_{12}) is the pharmaceutical form of cobalamin which can be converted to the active coenzymes, methylcobalamin and 5'-deoxyadenosylcobalamin. These coenzymes are necessary for folic acid metabolism, conversion of coenzyme A, and myelin synthesis. For example, methylcobalamin catalyzes the demethylation of a folate cofactor which is involved in DNA synthesis. A lack of demethylation may result in folic acid deficiency. RDA, at 159-160. A deficiency of vitamin B_{12} was observed in chronic renal failure patients and dialysis patients. In addition, slow nerve conduction velocities were also noted in dialysis patients. Rostand, 29 AM. J. CLIN. RES. 691-697 (1976). Based on these observations, vitamin B_{12} supplementation may be appropriate as a means to compensate for any deficiency.

Furthermore, since vitamin B_{12} has a role in folic acid metabolism, supplementation may be effective in managing homocysteine levels in renal patients. Thus, the novel compositions of the present invention may comprise cyanocobalamin preferably in the amount ranging from about 10.8 to about 13.2 μg.

Biotin acts a coenzyme for a number of carboxylases and thus, has an important role in gluconeogenesis, fatty acid metabolism, and amino acid metabolism. RDA, at 166. It has been shown that biotin inhibits the effects of uremic toxins on tubulin polymerizaton. Braguer et al., 57 NEPHRON 192-196 (1991). Furthermore, there is some evidence to suggest that chronic renal failure patients and dialysis patients are at a risk for the development of a biotin deficiency. Mackenzie et al., 5 PROC. EUR. DIAL. TRANSPLANT. ASSOC. 172-178 (1968). In several dialysis patients diagnosed with uremic encephalopathy and neuropathy, symptoms of these disorders were alleviated by administration of biotin. Yatzidis et al., 305 N. ENGL. J. MED. 764 (1981). Thus, to maintain appropriate biotin levels in renal patients, one embodiment of the compositions of the present invention may comprise biotin preferably in an amount ranging from about 270 to about 330 μg.

Folic acid in its active form, tetrahydrofolate, is a coenzyme that is involved in the transfer of methyl groups and it plays a role in DNA synthesis, purine synthesis, and amino acid synthesis, such as the conversion of glycine to serine and the transformation of homocysteine to methionine. The activation of folic acid requires a vitamin B_{12}-dependent transmethylation and vitamin B_{12} is also necessary for folic acid delivery to tissues. RDA, at 150. The metabolism of folic acid is altered by uremia and the absorption of tetrahydrofolate is impaired in chronic renal failure patients. Said et al., 6 ACTA VITAMINOL. ENZYMOL. 339-346 (1984). Furthermore, the diet generally prescribed for renal patients tends to be low in folic acid content and medications used by chronic renal failure patients may also inhibit the activity of folic acid. Stein et al., 3 BLOOD PURIF. 52-62 (1985); Cunningham et al., 282 BR. MED. J. 1582 (1981). The high incidence of homocysteinemia observed in chronic renal failure patients and the related risk of development of atherosclerosis suggest that folic acid supplementation may provide an effective method for managing this condition and also provide a cardio-protective effect. Robinson et al., 94 CIRCULATION 2743-2748 (1996). Therefore, in a preferred embodiment, the compositions of the present invention may comprise folic acid preferably in the amount ranging from about 2.25 to about 2.75 mg.

Diabetic nephropathy is a leading cause of end-stage renal disease with Type II diabetes comprising the largest disease group requiring renal support. Ibrahim et al., 13 BAILLIERES CLIN. ENDOCRINOL. METABOL. 239-264 (1999). The trace mineral, chromium, may promote insulin activity by increasing insulin binding and insulin receptor number. Chromium also activates the insulin receptor kinase leading to increased insulin sensitivity. Anderson et al., 26 DIABETES METABOL. 22-27 (2000). It is estimated that 90% of adults in the United States consume less than the recommended minimum amount of chromium. In addition, the typical renal diet is likely to be further restricted in chromium content. NUTRITION CONCEPTS AND CONTROVERSIES 293 (Sizer et al., 8th ed.). Hence, to maintain appropriate chromium levels in renal patients, one embodiment of the compositions of the present invention may comprise chromium preferably in the amount ranging from about 180 to about 220 μg.

Selenium is a component of the antioxidant enzyme, glutathione peroxidase, which plays a critical role in the control of oxygen metabolism, particularly catalyzing the breakdown of hydrogen peroxide. Burk, 3 ANNU. REV. NUTR. 53-70 (1983). Glutathione peroxidase prevents the generation of free radicals and decreases the risk of oxidative damage to numerous tissues, including the vascular system. Holben, 99 J. AM. DIET. ASSOC. 836-843 (1999). Diabetic patients have even higher levels of oxidative stress due to the combination of diabetes and renal disease. Kedziora-Kornatowska, et al., 11 NEPHROL. DIAL. TRANSPLANT. 2829-2832 (1998). Selenium may be lost during dialysis therapy and dietary selenium may be less than adequate due to protein restrictions. Several studies have demonstrated significant decreases in serum selenium, selenium-dependent enzymes, and increased lipid peroxidation in dialysis patients. Smith et al., 7 J. RENAL NUTR. 69-72 (1997); Zima et al., 16 BLOOD PURIF. 253-260 (1998). Oral and intravenous selenium supplementation has proven to be effective in improving the selenium status and immune function of renal patients, while decreasing the levels of oxidative stress products. Temple et al., 10 J. RENAL NUTR. 16 (2000). Therefore, in a preferred embodiment, the compositions of the present invention may comprise selenium preferably in amounts ranging from about 63 to about 77 μg.

There are more than 200 zinc metalloenzymes including aldolase, alcohol dehydrogenase, RNA polymerase, and protein kinase C. Thus, zinc plays a role in numerous metabolic activities such as nucleic acid production, protein synthesis, and development of the immune system. Zima et al., 17 BLOOD PURIF. 182-186 (1999). Several studies have shown decreased serum

levels of zinc in dialysis patients and patients with renal failure. Thomson et al., 23 KIDNEY INT. 9-14 (1983); Muirhead et al., 6 AM. J. NEPHROL. 422-426 (1986). Zinc supplementation has been shown to improve a number of clinical symptoms observed in renal patients such as dygeusia, nerve conduction velocity, and impotency, and it has been proposed that zinc supplementation may restore impaired cell-mediated immunity and lymphocyte function. Zima et al., 17 BLOOD PURIF. 182-186 (1999). One embodiment of the compositions of the present invention provides a supplemental dose of zinc, preferably in the amount of about 18 to about 22 mg.

The compositions of the present invention are preferably administered in amounts to patients that provide the supplementation required to alleviate the vitamin and mineral deficiencies associated with renal disease. In a preferred embodiment of the present invention, the composition comprises 50 mg of vitamin C, 35 IU vitamin E, 3 mg of thiamine, 2 mg of riboflavin, 20 mg of niacin, 10 mg of pantothenic acid, 15 mg of pyridoxine, 12 μg cyanocobalamin, 300 μg of biotin, 2.5 mg of folic acid, 200 μg of chromium, 70 μg of selenium, and 20 mg of zinc.

In a further preferred embodiment, the composition comprises about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.7 mg to 3.3 mg thiamine (vitamin B_1), 1.8 mg to 2.25 mg riboflavin (vitamin B_2), 18 mg to 22 mg niacin (vitamin B_3), 9 mg to 11 mg pantothenic acid (vitamin B_5), 13.5 mg to 16.5 mg pyridoxine (vitamin B_6), 10.8 μg to 13.2 μg cyanocobalamin (vitamin B_{12}), 270 μg to 330 μg biotin, 2.25 mg to 2.75 mg folic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, and 18 mg to 22 mg zinc.

A preferred dosage of the compositions of the present invention may consist of one or more caplets for human oral consumption. If more than one caplet is used, each individual caplet may be identical to the other caplets, or each may contain only some of the ingredients of the composition, so that the combination of the different caplets comprises a composition of the present invention.

The compositions of the present invention represent a combination of essential vitamins and minerals that work together with various metabolic systems and physiological responses of the human body. The ingredients of the present invention are preferably combined into a composition which may be in the form of a solid powder, caplets, tablets, lozenges, pills, capsules, or a liquid, and which may be administered alone or in suitable combination with other

components. For example, the composition of the present invention may be administered in one or more caplets or lozenges as practical for ease of administration. Each of the vitamins and minerals is commercially available, and can be blended to form a single composition or can form multiple compositions which may be co-administered.

To prepare the components of the present invention, each of the active ingredients may be combined in intimate admixture with a suitable carrier according to conventional compounding techniques. This carrier may take a wide variety of forms depending upon the form of the preparation desired for administration, *e.g.*, oral, sublingual, nasal, topical patch, or parenteral. The composition may comprise one to three caplets or lozenges, the composition of each being identical to each other caplet or lozenge.

In preparing the composition in oral dosage form, any of the usual media may be utilized. For liquid preparations (*e.g.*, suspensions, elixirs, and solutions) media containing for example water, oils, alcohols, flavoring agents, preservatives, coloring agents and the like may be used. Carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like may be used to prepare oral solids (*e.g.*, powders, caplets, pills, tablets, capsules, and lozenges). Controlled release forms may also be used. Because of their ease in administration, caplets, tablets, pills, and capsules represent the most advantageous oral dosage until form, in which case solid carriers are employed. If desired, tablets may be sugar coated or enteric coated by standard techniques.

The present invention also relates to methods for supplementing nutritional deficiencies in a patient. Specifically, the present invention relates to methods for supplementing the nutritional deficiencies in a patient comprising the step of administering to said patient compositions comprising vitamin C, vitamin E, B-complex vitamins, chromium, selenium, and zinc.

In a preferred embodiment of the present invention, the methods for supplementing nutritional deficiencies in a patient or person in need thereof, comprise the step of administering to said patient the composition comprising 50 mg of vitamin C, 35 IU vitamin E, 3 mg of thiamine, 2 mg of riboflavin, 20 mg of niacin, 10 mg of pantothenic acid, 15 mg of pyridoxine, 12 μg cyanocobalamin, 300 μg of biotin, 2.5 mg of folic acid, 200 μg of chromium, 70 μg of selenium, and 20 mg of zinc.

In a further preferred embodiment, the methods of the present invention comprise administering to a patient compositions comprising about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.7 mg to 3.3 mg thiamine (vitamin B_1), 1.8 mg to 2.25 mg riboflavin (vitamin B_2), 18 mg to 22 mg niacin (vitamin B_3), 9 mg to 11 mg pantothenic acid (vitamin B_5), 13.5 mg to 16.5 mg pyridoxine (vitamin B_6), 10.8 μg to 13.2 μg cyanocobalamin (vitamin B_{12}), 270 μg to 330 μg biotin, 2.25 mg to 2.75 mg folic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, and 18 mg to 22 mg zinc.

These methods also preferably compromise the administration of one or more of the compositions of the present invention to a patient afflicted with renal disease or renal insufficiency. In a preferred embodiment of the present invention, the methods preferably compromise the administration of one or more of the compositions to a patient suffering from end-stage renal disease and undergoing dialysis treatment. In a further preferred embodiment, the methods preferably comprise the administration of one or more of the compositions of the present invention to treat the nutritional deficiencies of any disease state that results in increased oxidative stress, elevated cholesterol levels, or elevated homocysteine levels.

Other objectives, features and advantages of the present invention will become apparent from the following specific examples. The specific examples, while indicating specific embodiments of the invention , are provided by way of illustration only. Accordingly, the present invention also includes those various changes and modifications within the spirit and scope of the invention that may become apparent to those skilled in the art from this detailed description.

The invention will be further illustrated by the following non-limiting examples.

Example 1

A composition of the following formulation was prepared in caplet form by standard methods known to those skilled in the art:

Ascorbic acid	50 mg
Biotin	300 µg
Cyanocobalamin	12 µg
d-Alpha Tocophenyl Succinate	35 IU
d-Calcium Pantothenate	10 mg
Folic acid	2.5 mg
Niacinamide	20 mg
Pyridoxine	15 mg
Riboflavin	2 mg
Thiamine	3 mg
Chromium Chloride	200 µg
L-Selenomethionine	70 µg
L-Optizinc ZML-200 Inter-Health	20 mg

One (1) caplet per day is the recommended dosage or as recommended by physician.

Example 2

A study is undertaken to evaluate the effectiveness of the composition of the present invention in the treatment of patients diagnosed with end-stage renal disease (ESRD). The objective of the study is to determine whether oral intake of the composition results in an improvement of the nutritional status of the patient.

A double-blind, placebo controlled study is conducted over a twelve-month period. A total of sixty subjects (30 men and 30 women) aged 40 to 85 years, suffering from ESRD, are chosen for the study. An initial assessment of nutritional status is conducted utilizing methods such as the peroxide hemolysis test to assess vitamin E deficiency, measurement of erythrocyte transketolase activity to determine thiamine levels, determination of erythrocyte glutathione reductase activity to assess riboflavin status, and high performance liquid chromatography to directly measure PLP and pyridoxine levels.

The sixty subjects are separated into two separate groups of fifteen men and fifteen women. In the first group, each subject is administered 1 to 2 caplets, daily, of the composition as described in example 1. In the second group (control) each subject is administered 1 to 2 placebo caplets, daily.

An assessment of nutritional status for each subject is measured at one-month intervals for a twelve month period as described above and the data is evaluated using multiple linear regression analysis and a standard students t-test. In each analysis the baseline value of the outcome variable is included in the model as a covariant. Treatment by covariant interaction effects is tested by the method outlined by Weigel & Narvaez, 12 CONTROLLED CLINICAL TRIALS 378-94 (1991). If there are no significant interaction effects, the interaction terms are removed from the model. The regression model assumptions of normality and homogeneity of variance of residuals are evaluated by inspection of the plots of residuals versus predicted values. Detection of the temporal onset of effects is done sequentially by testing for the presence of significant treatment effects at 18, 12, and 6 weeks, proceeding to the earlier time in sequence only when significant effects have been identified at each later time period. Changes from the baseline within each group are evaluated using paired t-tests. In addition, analysis of variance is performed on all baseline measurements and measurable subject characteristics to assess homogeneity between groups. All statistical procedures are conducted using the Statistical

Analysis System (SAS Institute Inc., Cary, NC). An alpha level of 0.05 is used in all statistical tests.

A statistically significant improvement in the nutritional status is observed in the treated subjects upon completion of the study but not the controls. The differences between nutritional state in the treated subjects and controls are statistically significant. Therefore, the study confirms that oral administration of the composition of the present invention is effective in the treatment of patients diagnosed with ESRD.

We claim:

1. A composition for supplementing nutritional deficiencies in a patient or person in need thereof, comprising vitamin C, vitamin E, chromium, selenium, zinc, and B-complex.

2. The composition of claim 1, wherein said patient is afflicted with kidney disease.

3. The composition of claim 2, wherein said kidney disease is end-stage renal disease.

4. The composition of claim 1, wherein said patient is suffering from renal insufficiency.

5. The composition of claim 1, wherein said patient is undergoing dialysis therapy.

6. The composition of claim 1, wherein said nutritional deficiencies are a result of dietary restrictions.

7. The composition of claim 1, wherein said nutritional deficiencies are a result of a disease state.

8. The composition of claim 7, wherein said disease state is kidney disease.

9. The composition of claim 8, wherein said kidney disease is end-stage renal disease.

10. The composition of claim 1, wherein said nutritional deficiencies are a result of dialysis therapy.

11. The composition of claim 1, wherein said disease state leads to increased oxidative stress in said patient.

12. The composition of claim 1, wherein said disease state leads to elevated cholesterol levels in said patient.

13. The composition of claim 1, wherein said disease state leads to elevated homocysteine levels in said patient.

14. The composition of claim 1, wherein said vitamin C comprises ascorbic acid.

15. The composition of claim 1, wherein said vitamin E comprises d-alpha tocopheryl succinate.

16. The composition of claim 1, wherein said chromium is selected from one or more of the group consisting of chromium chloride, chromium picolinate, and chromium tripicolinate.

17. The composition of claim 16 wherein said chromium comprises chromium chloride.

18. The composition of claim 1, wherein said selenium comprises L-selenomethionine.

19. The composition of claim 1, wherein said zinc comprises L-Optizinc ZML-200 Inter-Health™.

20. The composition of claim 1, wherein said B-complex is one or more vitamins selected from the group consisting of pantothenic acid, cyanocobalamin, niacin, pyridoxine, riboflavin, thiamine, folic acid, and biotin.

21. The composition of claim 20, wherein said folic acid is in the range of about 2.25 mg to 2.75 mg.

22. The composition of claim 20, wherein said biotin is in the range of about 270 μg to 330 μg.

23. The composition of claim 20, wherein said pantothenic acid is in the range of about 9 mg to 11.

24. The composition of claim 20, wherein said cyanocobalamin is in the range of about 10.8 μg to 13.2 μg.

25. The composition of claim 20, wherein said niacin is in the range of about 18 mg to 22 mg.

26. The composition of claim 20, wherein said pyridoxine is in the range of about 13.5 mg to 16.5 mg.

27. The composition of claim 20, wherein said riboflavin is in the range of about 1.8 mg to 2.2 mg.

28. The composition of claim 20, wherein said thiamine is in the range of about 2.7 mg to 3.3 mg.

29. The composition of claim 20, wherein said pantothenic acid comprises d-calcium pantothenate.

30. The composition of claim 20, wherein said niacin comprises niacinamide.

31. The composition of claim 1, wherein said vitamin C is in the range of about 45 mg to 55 mg.

32. The composition of claim 1, wherein said vitamin E is in the range of about 31.5 IU to 38.5 IU.

33. The composition of claim 1, wherein said chromium is in the range of about 180 μg to 220 μg.

34. The composition of claim 1, wherein said selenium is in the range of about 63 μg to 77 μg.

35. The composition of claim 1 wherein said zinc is in the range of about 18 mg to 22 mg.

36. The composition of claim 1, wherein said d-alpha tocopheryl succinate is in the range of about 31.5 IU to 38.5 IU.

37. A composition for supplementing nutritional deficiencies in a patient or person in need thereof, comprising about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.25 mg to 2.75 mg folic acid, 270 μg to 330 μg biotin, 9 mg to 11 mg pantothenic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, 18 mg to 22 mg zinc, 18 mg to 22 mg niacin, 13.5 mg to 16.5 mg pyridoxine, 1.8 mg to 2.25 mg riboflavin, 10.8 μg to 13.2 μg cyanocobalamin, and 2.7 mg to 3.3 mg thiamine.

38. The composition of claim 37, wherein said composition comprises 50 mg of vitamin C, 35 IU vitamin E, 2.5 mg of folic acid, 300 μg of biotin, 10 mg of pantothenic acid, 200 μg of chromium, 70 μg of selenium, 20 mg of zinc, 20 mg of niacin, 15 mg of pyridoxine, 2 mg of riboflavin, 12 μg cyanocobalamin, and 3 mg of thiamine.

39. The composition of claim 37, wherein said composition is administered to said patient daily.

40. The composition of claim 37, wherein said composition is administered to said patient orally.

41. The composition of claim 37, wherein said composition further comprises a pharmaceutically acceptable carrier.

42. The composition of claim 37, wherein said composition is administered to a patient suffering from kidney disease.

43. The composition of claim 42, wherein said kidney disease is end-stage renal disease.

44. The composition of claim 37, wherein said composition is administered to a patient suffering from renal insufficiency.

45. The composition of claim 37, wherein said composition is administered to patient undergoing dialysis therapy.

46. The composition of claim 37, wherein said nutritional deficiencies are a result of dietary restrictions.

47. The composition of claim 37, wherein said nutritional deficiencies are a result of a disease state.

48. The composition of claim 47, wherein said disease state is kidney disease.

49. The composition of claim 48, wherein said kidney disease is end-stage renal disease.

50. The composition of claim 37, wherein said nutritional deficiencies are a result of dialysis therapy.

51. The composition of claim 37, wherein said disease state leads to increased oxidative stress in said patient.

52. The composition of claim 37, wherein said disease state leads to elevated cholesterol levels in said patient.

53. A method for supplementing nutritional deficiencies in a patient comprising the step of administering to said patient a composition comprising vitamin C, vitamin E, chromium, selenium, zinc, and B-complex.

54. The method of claim 53, wherein said patient is afflicted with kidney disease.

55. The method of claim 53, wherein said kidney disease is end-stage renal disease.

56. The method of claim 53, wherein said patient is suffering from renal insufficiency.

57. The method of claim 53 wherein said patient is undergoing dialysis therapy.

58. The method of claim 53, wherein said vitamin C comprises ascorbic acid.

59. The method of claim 53, wherein said vitamin E comprises d-alpha tocopheryl succinate.

60. The method of claim 53, wherein said chromium is selected from one or more of the group consisting of chromium chloride, chromium picolinate, and chromium tripicolinate.

61. The method of claim 60, wherein said chromium comprises chromium chloride.

62. The method of claim 53, wherein said selenium comprises L-selenomethionine.

63. The method of claim 53, wherein said zinc comprises L-Optizinc ZML-200 Inter-Health™.

64. The method of claim 53, wherein said B-complex is one or more vitamins selected from the group consisting of pantothenic acid, cyanocobalamin, niacin, pyridoxine, riboflavin, thiamine, folic acid, and biotin.

65. The method of claim 64, wherein said pantothenic acid comprises d-calcium pantothenate.

66. The method of claim 64, wherein said niacin comprises niacinamide.

67. The method of claim 64, wherein said folic acid is in the range of about 2.25 mg to 2.75 mg.

68. The method of claim 64, wherein said biotin is in the range of about 270 µg to 330 µg.

69. The method of claim 64, wherein said pantothenic is in the range of about 9 mg to 11 mg.

70. The method of claim 64, wherein said cyanocobalamin is in the range of about 10.8 µg to 13.2 µg.

71. The method of claim 64, wherein said niacin is in the range of about 18 mg to 22 mg.

72. The method of claim 64, wherein said pyridoxine is in the range of about 13.5 mg to 16.5 mg.

73. The method of claim 64, wherein said riboflavin is in the range of about 1.8 mg to 2.2 mg.

74. The method of claim 64, wherein said thiamine is in the range of about 2.7 mg to 3.3 mg.

75. The method of claim 53, wherein said vitamin C is in the range of about 45 mg to 55 mg.

76. The method of claim 53, wherein said vitamin E is in the range of about 31.5 IU to 38.5 IU.

77. The method of claim 53, wherein said chromium is in the range of about 180 µg to 220 µg.

78. The method of claim 53, wherein said selenium is in the range of about 63 µg to 77 µg.

79. The method of claim 53, wherein said zinc is in the range of about 18 mg to 22 mg.

80. The method of claim 53, wherein said alpha-tocopheryl is in the range of about 31.5 IU to 38.5 IU.

81. The composition of claim 53, wherein said nutritional deficiencies are a result of dietary restrictions.

82. The composition of claim 53, wherein said nutritional deficiencies are a result of a disease state.

83. The composition of claim 82, wherein said disease state is kidney disease.

84. The composition of claim 53, wherein said kidney disease is end-stage renal disease.

85. The composition of claim 53, wherein said nutritional deficiencies are a result of dialysis therapy.

86. The composition of claim 53, wherein said disease state leads to increased oxidative stress in said patient.

87. The composition of claim 53, wherein said disease state leads to elevated cholesterol levels in said patient.

88. A method for supplementing nutritional deficiencies in a patient or person in need thereof, comprising the step of administering to said patient a composition comprising about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.25 mg to 2.75 mg folic acid, 270 μg to 330 μg biotin, 9 mg to 11 mg pantothenic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, 18 mg to 22 mg zinc, 18 mg to 22 mg niacin, 13.5 mg to 16.5 mg pyridoxine, 1.8 mg to 2.25 mg riboflavin, 10.8 μg to 13.2 μg cyanocobalamin, and 2.7 mg to 3.3 mg thiamine.

89. The method of claim 88, wherein said composition comprises 50 mg of vitamin C, 35 IU vitamin E, 2.5 mg of folic acid, 300 μg of biotin, 10 mg of pantothenic acid, 200 μg of chromium, 70 μg of selenium, 20 mg of zinc, 20 mg of niacin, 15 mg of pyridoxine, 2 mg of riboflavin, 12 μg cyanocobalamin, and 3 mg of thiamine.

90. The method of claim 88, wherein said composition further comprises pharmaceutically acceptable carrier.

91. The method of claim 88, wherein said patient is suffering from kidney disease.

92. The method of claim 91, wherein said kidney disease is end-stage renal disease.

93. The method of claim 88, wherein said patient is suffering from renal insufficiency.

94. The method of claim 88, wherein said patient is undergoing dialysis therapy.

95. The composition of claim 88, wherein said nutritional deficiencies are a result of dietary restrictions.

96. The composition of claim 88, wherein said nutritional deficiencies are a result of a disease state.

97. The composition of claim 96, wherein said disease state is kidney disease.

98. The composition of claim 97, wherein said kidney disease is end-stage renal disease.

99. The composition of claim 88, wherein said nutritional deficiencies are a result of dialysis therapy.

100. The composition of claim 88, wherein said disease state leads to increased oxidative stress in said patient.

101. The composition of claim 88, wherein said disease state leads to elevated cholesterol levels in said patient.

102. A method for supplementing nutritional deficiencies in a patient suffering from kidney disease comprising the step of administering to said patient a composition comprising about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.25 mg to 2.75 mg folic acid, 270 μg to 330 μg biotin, 9 mg to 11 mg pantothenic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, 18 mg to 22 mg zinc, 18 mg to 22 mg niacin, 13.5 mg to 16.5 mg pyridoxine, 1.8 mg to 2.25 mg riboflavin, 10.8 μg to 13.2 μg cyanocobalamin, and 2.7 mg to 3.3 mg thiamine.

103. The method of claim 102, wherein said composition comprises 50 mg of vitamin C, 35 IU vitamin E, 2.5 mg of folic acid, 300 μg of biotin, 10 mg of pantothenic acid, 200 μg of chromium, 70 μg of selenium, 20 mg of zinc, 20 mg of niacin, 15 mg of pyridoxine, 2 mg of riboflavin, 12 μg cyanocobalamin, and 3 mg of thiamine.

104. The method of claim 102, wherein said composition further comprises pharmaceutically acceptable carrier.

105. The method of claim 102, wherein said composition is administered to said patient daily.

106. The method of claim 102, wherein said composition is administered to said patient orally.

107. A method for supplementing nutritional deficiencies in a patient suffering from end-stage renal disease comprising the step of administering to said patient a composition comprising about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.25 mg to 2.75 mg folic acid, 270 μg to 330 μg biotin, 9 mg to 11 mg pantothenic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, 18 mg to 22 mg zinc, 18 mg to 22 mg niacin, 13.5 mg to 16.5 mg pyridoxine, 1.8 mg to 2.25 mg riboflavin, 10.8 μg to 13.2 μg cyanocobalamin, and 2.7 mg to 3.3 mg thiamine.

108. The method of claim 107, wherein said composition comprises 50 mg of vitamin C, 35 IU vitamin E, 2.5 mg of folic acid, 300 μg of biotin, 10 mg of pantothenic acid, 200 μg of chromium, 70 μg of selenium, 20 mg of zinc, 20 mg of niacin, 15 mg of pyridoxine, 2 mg of riboflavin, 12 μg cyanocobalamin, and 3 mg of thiamine.

109. The method of claim 107, wherein said composition further comprises a pharmaceutically acceptable carrier.

110. The method of claim 107, wherein said composition is administered to said patient daily.

111. The method of claim 107, wherein said composition is administered to said patient orally.

112. A method for supplementing nutritional deficiencies in a patient suffering undergoing dialysis therapy comprising the step of administering to said patient a composition comprising about 45 mg to 55 mg vitamin C, 31.5 IU to 38.5 IU vitamin E, 2.25 mg to 2.75 mg folic acid, 270 μg to 330 μg biotin, 9 mg to 11 mg pantothenic acid, 180 μg to 220 μg chromium, 63 μg to 77 μg selenium, 18 mg to 22 mg zinc, 18 mg to 22 mg niacin, 13.5 mg to 16.5 mg

pyridoxine, 1.8 mg to 2.25 mg riboflavin, 10.8 μg to 13.2 μg cyanocobalamin, and 2.7 mg to 3.3 mg thiamine.

113. The method of claim 112, wherein said composition comprises 50 mg of vitamin C, 35 IU vitamin E, 2.5 mg of folic acid, 300 μg of biotin, 10 mg of pantothenic acid, 200 μg of chromium, 70 μg of selenium, 20 μg of zinc, 20 mg of zinc, 20 mg of niacin, 15 mg of pyridoxine, 2 mg of riboflavin, 12 μg cyanocobalamin, and 3 mg of thiamine.

114. The method of claim 112, wherein said composition further comprises pharmaceutically acceptable carrier.

115. The method of claim 112, wherein said composition is administered to said patient daily.

116. The method of claim 112, wherein said composition is administered to said patient orally.

ABSTRACT

The present invention relates to compositions and methods for treating the nutritional deficiencies observed in patients suffering from renal disease and associated disorders. Specifically, the method involves administering to a renal patient a composition comprising vitamin C, vitamin E, the B-complex vitamins, chromium, selenium, and zinc.

DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

METHOD AND COMPOSITION FOR SUPPLEMENTATION OF NUTRITIONAL DEFICIENCIES IN RENAL PATIENTS

the specification of which is attached hereto unless the following box is checked:

☐ was filed on _____ as United States Application _____ and was amended on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate, or § 365(a) of any PCT International application which designated at least one country other than the United States, listed below and have also identified below any foreign application for patent or inventor's certificate, or PCT International application having a filing date before that of the application on which priority is claimed:

PRIOR FOREIGN APPLICATION(S)

NUMBER	COUNTRY	DAY/MONTH/YEAR FILED	PRIORITY CLAIMED

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below.

APPLICATION NO.	FILING DATE

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s), or § 365(c) of any PCT International application designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I

acknowledge the duty to disclose information which is known by me to be material to patentability as defined in Title 37, Code of Federal Regulations § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application:

APPLICATION SERIAL NO.	FILING DATE	STATUS: PATENTED, PENDING, ABANDONED

I hereby appoint as my attorneys, with full powers of substitution and revocation, to prosecute this application and transact all business in the Patent and Trademark Office connected therewith: Don J. Pelto, Reg. No. 33,754, Jeff E. Schwartz, Reg. No. 39,019, Mary S. Jones, Reg. No. 37,156, and Christina Annick, Reg. No. 46,428.

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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